

What is claimed is:

1. A method of making a suspended or soluble protein conjugate, the method comprising the steps of:

- a) providing a reactive surface, protein that is capable of forming a stable, disruptable bond with the reactive solid-surface, and a Second Macromolecule,
- b) contacting the protein to the reactive solid-surface to form a surface-bound protein complex,
- c) if necessary, activating the protein, or Second Macromolecule, or both,
- d) contacting the surface bound protein with a reactive Second Macromolecule to form a solid-surface:protein:Second Macromolecule stable complex,
- e) disrupting the stable bond between the solid-surface and the protein conjugate in a liquid medium to yield a suspended or soluble protein conjugate comprising the protein and the Second Macromolecule.

2. A method of making a suspended or soluble Macromolecular Conjugate, the method comprising the steps of:

- a) providing a reactive surface,
- b) providing a First Macromolecule that is capable of forming a stable, disruptable bond with the reactive solid-surface,
- c) contacting the First Macromolecule to the reactive solid-surface to form a surface-bound First Macromolecule complex,
- d) if necessary, activating the First Macromolecule, or Second Macromolecule, or both,
- e) contacting the surface bound First Macromolecule with a reactive Second Macromolecule to form a solid-surface:First Macromolecule:Second Macromolecule stable complex,
- f) disrupting the stable bond between the solid-surface and the First Macromolecule conjugate in a liquid medium to yield a suspended or soluble Macromolecular Conjugate comprising the First Macromolecule and the Second Macromolecule,

wherein the First Macromolecule comprises a plurality of reactive moieties capable of interacting with the Second Macromolecule, and the Second Macromolecule comprises a plurality of reactive moieties capable of interacting with the First Macromolecule.

3. The method of claim 2, wherein the First Macromolecule is bound to the solid-surface through a disruptable covalent bond.

4. The method of claim 2, wherein Second Macromolecule is attached to the First Macromolecule through a bifunctional linker.

5. The method of claim 4, wherein the bifunctional linker is selected from the group consisting of N-Succinimidyl S-Acetylthiopropionate, N-Succinimidyl S-Acetylthioacetate, 2-Iminothiolane (Trauts reagent), 4-Succinimidylloxycarbonyl-Methyl-(2-Pyridyldithio)-Toluene Sulfosuccinimidyl, 4-[N-maleimidomethyl]-cyclohexane-1-carboxylate, N-[gamma-Maleimidobutyryloxy]sulfo-succinimide ester, N-(K-Maleimidoundecanoyloxy) Sulfosuccinimide Ester, Maleimidoacetic Acid N-Hydroxysuccinimide Ester, N-(Epsilon-Maleimidocaproic Acid) Hydrazide, N-(K-Maleimidoundecanoic Acid) Hydrazide, N-(Beta-Maleimidopropionic Acid) Hydrazide, and 3-(2-Pyridyldithio)Propionyl Hydrazide.

6. The method of claim 5, wherein the First Macromolecule is a protein, and the protein comprises reactive sulfhydryl moieties, and the solid-surface comprises maleimide moieties bound to the surface via hydrazone linkage.

7. The method of claim 4 further comprising:
rendering the solid-surface unreactive with the First Macromolecule after completing step (c).

8. The method of claim 7, further comprising
contacting the solid surface-bound: First Macromolecule: Second Macromolecule with a Third Macromolecule that is reactive with the Second Macromolecule to form a surface-bound complex comprising at least one unit of the Third Macromolecule linked to the First Macromolecule through the Second Macromolecule, wherein

the First Macromolecule and the Third Macromolecule may be the same or different.

9. The method of claim 8, further comprising

after contacting the Second Macromolecule with the Third Macromolecule: adding a deactivating reagent, or placing the surface-bound complex under conditions, sufficient to render any non-reacted reactive moieties on the Second Macromolecule in the complex non-reactive to the reactive moieties used on the Third Macromolecule,

removing any excess deactivating reagent, or altering the conditions, such that the reactive moieties on additional macromolecules added to the reaction would not be deactivated, and contacting the surface-bound complex with a Fourth Macromolecule under conditions sufficient to form a bond between the Third Macromolecule and the Fourth Macromolecule, wherein

the Second Macromolecule and the Fourth Macromolecule may be the same or different.

10. The method of claim 8, further comprising one or more sequential additions of macromolecules.

11. The method of claim 2, wherein the solid surface is selected from the group consisting of agarose, polyacrylamide, and polystyrene, the reactive moiety on the solid support is a maleimide linked to the support via a hydrazone group, the First Macromolecule is linked to the maleimide on the solid support via the thioether group formed by reaction of the sulfhydryl group with the maleimide group.

12. The method of claim 2, wherein the stable bond between the solid-surface and the First Macromolecule conjugate is disrupted by contacting the bond with a reagent specific to the disruptable bond, thereby releasing the conjugate from the solid surface.

13. The method of claim 12, wherein the disruption of the bond yields a hydrazide on the First Macromolecule of the Macromolecular Conjugate, the method further comprising reacting the hydrazide with a compound to change the character of the conjugate.

14. The method of claim 2, wherein a residual reactive moiety on the First Macromolecule or a residual reactive moiety on the Second Macromolecule that does not react to bond the First Macromolecule with the Second Macromolecule is deactivated with a capping compound.

15. The method of claim 15, wherein the capping compound is zwitterionic.

16. The method of claim 15, wherein the capping compound is a polymer selected from the group consisting of dextran, polyethylene glycol, and polysaccharides.

17. The method of claim 15, wherein the capping compound is polymer selected from the group consisting of a polypeptide and a nucleic acid.

18. The method of claim 2, wherein the First Macromolecule is provided in a composition comprising a second molecule that reacts with the solid surface and does not react with the Second Macromolecule.

19. A conjugate produced by the method of claim 1, wherein the conjugate comprises only one antibody.

20. A conjugate produced by the method of claim 1, wherein the conjugate comprises a predetermined number of antibodies, wherein the number of antibodies is between 2 and 30.

21. A composition comprising a population of conjugates, wherein each conjugate of the population comprises a single antibody.

22. A composition comprising a population of conjugates, wherein each conjugate of the population comprises a predetermined number of antibodies and the number of antibodies is between 2 and 30.

23. A conjugate comprising three layers of macromolecules, wherein at least two of the three layers comprise a plurality of macromolecules, and wherein the layers form a surface in three dimensions.

24. A conjugate comprising
a specific binding member,
a plurality of end-point molecules, and
a plurality of spacer molecules, wherein
the spacer molecules substantially separate the end-point molecules.

25. A population of conjugates, wherein
substantially each conjugate of the molecule comprises from 1 to 30 molecules of a specific binding members,
each of the specific binding members is disposed on the surface of the conjugate, and
substantially each conjugate comprises a core, wherein the core comprises at least one molecule that is not disposed on the surface of the conjugate.

26. A conjugate prepared according to claim 1 in which one of the macromolecules, preferably the first, comprises a chromophore rendering it optically distinguishable from the other macromolecules of the conjugate such that the final conjugate can be quantified according to the optical absorbance or fluorescence of said chromophore.

27. A conjugate according to claim 26, wherein the macromolecule is selected from the list R-phycoerythrin, B-phycoerythrin, and allophycocyanin.

28. A kit comprising a reactive conjugate complex, and a cleavage reagent wherein,
the reactive conjugate complex comprises a solid bonded with a First Macromolecule covalently complexed with a Reactive Macromolecule, and
the cleavage reagent is capable of cleaving the bond between the solid and the First Macromolecule.

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